REMARKS

Applicants respectfully request reconsideration of the present application.

SPECIFICATION

Applicants have amended the title of the application to correct an inadvertent typographical error. No new matter has been added.

CLAIMS STATUS

Applicants have amended claims 8, 34, 38 and 39 without prejudice or disclaimer to present the invention in a clearer manner. No new matter has been added.

After the amendment, claims 8, 11-13, 15-16, 18-34 and 38-39 are pending.

REJECTION UNDER 35 U.S.C. § 112 ¶ 2

Claim 34 stands rejected as incomplete for omitting essential steps. Applicants believe that the revised claim 34 obviates the rejection.

REJECTION UNDER 35 U.S.C. § 103(a)

Claims 8, 11-13, 15-16, 18-19, 22-26, 29-30, 32-34 and 38-39 stand rejected as obvious over SmithKline Beecham Co. (WO 95/06410 or the '410 document) in view of Sekine *et al.* (WO 97/28794 as translated by US 6,054,484) and RxList Monographs (1999). Applicants traverse the rejection.

The '410 document discloses angiotensin II receptor antagonist, 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, in claim 13 and topical administration of angiotensin II receptor antagonists on page 29, lines 14-32. However, as admitted by the PTO, the '410 document fails to teach a permeability regulator comprising (A) fatty acid ester, (B) polyol and (C) non-ionic surfactant, see Office Action, page 3. Furthermore, the '410 document does not provide any suggestion or motivation to use such a regulator for topical administration of angiotensin II receptor antagonists.

Sekine teaches compositions for transdermal delivery of diclofenac sodium. One of the Sekine's compositions, composition # 23, includes isopropyl myristate, propylene glycol and coconut fatty acid diethanolamide treated by the PTO as a fatty ester, a polyol and a non-ionic surfactant respectively. However, Sekine neither teaches 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, nor provides any suggestion or motivation to substitute diclofenac sodium with any other compound.

The PTO uses RxList as evidencing insolubility of 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate, which is also known as Candesartan cilexetil, in water. The PTO notes that Sekine teaches that "diclofenac sodium has 1.5% solubility in water" and concludes that "when formulating a compound that is poorly soluble in water such as Candesartan cilexetil into a transdermal delivery system, one of ordinary skill in the art could look to Sekine et al. as a method of formulating a compound that has poor solubility in water into a transdermal delivery device...", see Office Action, page 4.

In response, Applicants note that the PTO failed to establish a *prima facie* case of obviousness. As explained above, the '410 document does not provide any suggestion or motivation to use a permeability regulator comprising (A) fatty acid ester, (B) polyol and (C) non-ionic surfactant for topical administration of angiotensin II receptor antagonists and Sekine does not provide any suggestion or motivation to substitute diclofenac sodium with 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate in his transdermal composition.

Furthermore, contrary to the PTO's statement on page 4, one of ordinary skill in the art would not look to Sekine for formulating a transdermal composition of a compound practically insoluble in water, such as Candesartan cilexetil. Sekine himself teaches that diclofenac sodium has 1.5% solubility in water, which is far from being practically insoluble. To illustrate a difference in water solubility between Candesartan cilexetil and diclofenac sodium in more quantitative terms, Applicants submit a paper by Bartolomei *et al.* Journal of Pharmaceutical and Biomedical Analysis 40 (2006) 1105-1113, which presents a value of

solubility of diclofenac sodium in water as 2.61 mg/mL at 20 °C. For comparison, a solubility of Candesaratan cilexetil under the same conditions is less than < 0.00005 mg/mL. Taking into account more than 50,000 times difference in water solubilities between Candesartan cilexetil and diclofenac sodium, it is highly doubtful that one of ordinary skill in the art would consider Sekine for formulating a percutaneous absorption preparation for 1-(cyclohexyloxycarbonyloxy)ethyl 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]benzimidazole-7-carboxylate.

In conclusion, since the PTO failed to demonstrate that one ordinary skill in the art would have a required motivation and a required reasonable expectation of success to combine teachings of the '410 document and Sekine, Applicants respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to

charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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